Ciência Animal, v.32, n.3, p.200-208, jul./set., 2022.

CRYOSURGERY USING DIMETHYL ETHER IN THE TREATMENT OF PIGMENTARY KERATITIS IN PUG DOGS

(*Criocirurgia usando o dimethyl ether no tratamento da ceratite pigmentar em cães da raça Pug*)

Eduardo GHIGGI[1*]; Paula Stieven HÜNNING[2]; Maria Cristina Caldart de ANDRADE[2]; Gisele Pereira VALDETARO[3]; Tatiana MARTINEZ[4]; Rafael Kretzer CARNEIRO[5]

[1]Médico Veterinário Autônomo, Rua Humberto de Campos, 336, Lages/SC. CEP: 88.508-190; [2]Veterinária Autônoma, Porto Alegre/RS; [3]Veterinária autônoma, Vitória/ES; [4]Oftalmo Vet Colombia/Bogotá; [5]Universidade Estadual Paulista "Julio de Mesquita Filho". *E-mail: eduardo.ghiggi@gmail.com

ABSTRACT

Corneal pigmentation and vascularization eventually result in blindness in dogs. Pigmentary keratitis describes a relatively common presentation comprising the deposition of melanin in the cornea and conjunctival surface associated with chronic inflammation. Cryosurgery is indicated as a treatment for pigmentary keratitis in dogs. Due to melanocytes sensitivity to cold, cryosurgery is a viable treatment for severe refractory corneal pigmentation. The aim of this work was to evaluate the use of dimethyl ether in the treatment of pigmentary keratitis in 14 eyes of seven Pug dogs. Follow-up occurred after 30 days in four animals and six months in three animals. In all treated animals, there was a reduction in corneal pigmentation. Cryosurgery causes intracellular and extracellular ice crystal formation and other mechanisms that result in rupture and death of the melanocytes. The technique used was easy to perform, has a low cryogen cost and has few undesirable or serious side effects. However, after 30 days repigmentation occured in treated patients. Cryosurgery shows good results in the first four weeks, but partial recurrence occurred in all cases.

Keywords: *Surgery, eye, ophthalmology, canine.*

RESUMO

A pigmentação e a vascularização da córnea eventualmente resultam em cegueira em cães. A ceratite pigmentar é descrita com uma apresentação relativamente comum que compreende a deposição de melanina na córnea e na superfície conjuntival associada à inflamação crônica. A criocirurgia é indicada como tratamento para ceratite pigmentar em cães. Devido à sensibilidade dos melanócitos ao frio, a criocirurgia é um tratamento viável para pigmentação corneana refratária grave. O objetivo deste trabalho foi avaliar o uso do éter dimetílico no tratamento da ceratite pigmentar em 14 olhos de sete cães da raça Pug. O acompanhamento foi de 30 dias em quatro animais e seis meses em três animais. Em todos os animais tratados, houve redução da pigmentação da córnea. A criocirurgia causa a formação de cristais de gelo intracelular e extracelular e outros mecanismos que resultam na ruptura e morte dos melanócitos. A técnica utilizada foi de fácil execução, baixo custo de criogenia e poucos efeitos colaterais indesejáveis ou graves. No entanto, após 30 dias, ocorreu repigmentação nos pacientes tratados. A criocirurgia apresenta bons resultados nas primeiras quatro semanas, mas ocorreu recidiva parcial em todos os casos.

Palavras-chave: Cirurgia, olho, oftalmologia, canino, criocirurgia

INTRODUCTION

In 1924, pigmentary keratitis was first described by Nicholas, as an inflammatory or degenerative disease affecting the cornea of some breeds such as Pug, Pekinese and Poodle with dark pigment deposition on the cornea (VALLONE *et al*., 2017). Histologically, deposits of melanin occur in the corneal epithelium and stroma and tend to be progressive, spreading towards the central cornea and eventually leading to impaired vision. In patients that are

Recebido: mai./2022.
Publicado: set./2022.

nonresponsive to topical therapy, corneal pigmentation and vascularisation eventually result in blindness (ALLGOEWER and HOECHT, 2010). Pigmentary keratitis describes a relatively common presentation comprising the deposition of melanin in the cornea and conjunctival surface associated with chronic inflammation (VALLONE *et al*., 2017; MAINI *et al*., 2019).

In veterinary ophthalmology, cryosurgery has been used to treat pigmentary keratitis (HOLMBERG *et al*., 1986; STANLEY, 1988; AZOULAY, 2014). The known benefits of cryosurgery date back to 2500 BC, when the Egyptians used cold to soothe injuries (WEB FRAUNFELDER, 2008). Cryotherapy has been called cryocautery, cryothermy, and cryocoagulation, with cryogenic surgery and cryosurgery, utilising carbon dioxide, and nitrous oxide and liquid nitrogen being the most useful (MERIDETH and GELATT, 1980). However, dimethyl ether and tetrafluoroethane can also be used (FEATHERSTONE *et al*., 2009; AZOULAY, 2014).

The cryosurgical treatment of pigmentary keratitis was first proposed in 1986, when nine dogs of the German Shepherd breed that presented with pigmentary keratitis due to chronic superficial keratitis were treated. All dogs in that study showed clinical improvement (HOLMBERG *et al.,* 1986; STANLEY, 1988). Cryosurgery causes intracellular and extracellular ice crystal formation, pH changes, reduced blood flow, ischaemia and osmotic alterations that result in rupture and death of the cells (TEHRANI and FRAUNFELDER, 2013). The aim of this work was to evaluate dimethyl ether in the treatment of pigmentary keratitis in Pug dogs.

PATIENT CARE

Seven Pugs dogs (14 eyes) with pigmentary keratitis were included in this study, four females and three males all neutered with a median age of 7.8 years (range 5–9 years). Complete ophthalmic evaluation was performed including the Schirmer tear test (STT), fluorescein stain (Fluorescein Stripes, Ophthalmos, SP, Brazil), slit lamp (Portable Slit Lamp, Kowa SL15, Japan), and rebound tonometry (Tonovet®, Helsinki, Finland). When possible, indirect binocular ophthalmoscopy (Topcon®, Japan) and ocular ultrasonography (Vivid E, GE, USA) were performed prior to cryosurgery. Posterior examination of the patients was made with fluorescein stain and corneal photographs to evaluate reduction of the pigment on days 1, 7, 14 and 28 in four animals. Three animals that were followed-up for six months returned for monthly ophthalmic examination.

This case report was carried out following the norms of the Association for Research in Vision and Ophthalmology (ARVO) statement on the use of animals in ophthalmic and vision research. The owners provided signed consent. All animals in the present study were submitted to general anaesthesia with pre-anaesthetic medication of 0.3mg/kg intramuscular methadone (Mytedom, Cristália – São Paulo, Brazil), after 15 minutes they were submitted to anaesthetic induction with 5mg/kg of propofol (Propovan, Cristália – São Paulo, Brazil) and anaesthetic maintenance with isoflurane (Isoforine, Cristália – São Paulo, Brazil). Anaesthetic eye drops of tetracaine 1% in combination with phenylephrine 0.1% (Colírio Anestésico, Allergan, Brazil) were instilled 15 minutes before and one drop during the anaesthetic procedure. The animals were placed in lateral decubitus and mechanical blepharostasis using a blepharostat.

Recebido: mai./2022.
Publicado: set./2022.

Centralization of the ocular bulb was conducted with repair sutures (nylon 4-0) in four quadrants for adequate exposition of the entire cornea.

All dogs had progressive corneal pigmentation despite long-term topical anti-inflammatory treatment with tacrolimus 0.03% eye drops. All animals that participated in the study were of the Pug dog breed. They had keratoconjunctivitis sicca (STT less than 10 mm in 1 minute) and medial canthal entropion, which is characteristic of this breed. In the present study, the cryosurgical technique established by AZOULAY in 2014 was used. However, we selected only Pug dogs. Schematic division of the cornea into sectors (Fig. 01) was used as a form of registering corneal pigmentation pre and post-surgery.

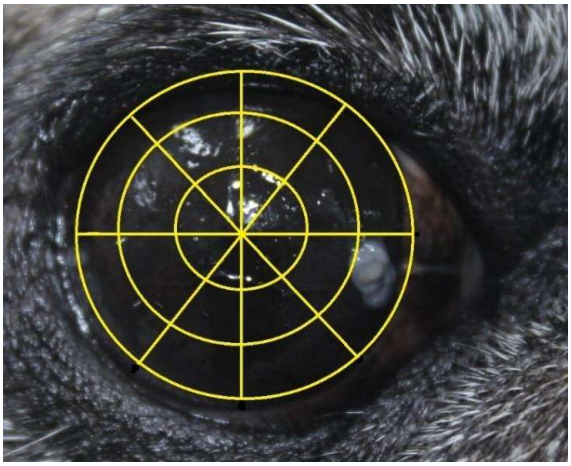

Figure 01: Eye image of a canine. Division of the cornea into 24 sectors for documentation of corneal pigmentation. (**Fonte:** Autoria própria, 2021)

The methodology was made to evaluate extension and density of corneal pigmentation, as well as vascularisation following a model already described (ALLGOEWER and HOECHT, 2010; AZOULAY, 2014). Similarly, the cornea was divided into 24 sectors for documentation of its pigmentation. In turn, the extent of pigmentation was scored in each sector (0 = no pigmentation; 1 = pigmented area <30% of the sector area; 2 = pigmented area >30–60% of the sector area; 3 = pigmented area >60%).

Posteriorly, the cryosurgery was performed with dimethyl ether (Pointts®, Genomma Laboratories do Brazil, LTDA) originally designed for dermatological use. The kit contains an aerosol bottle of liquid cryogen (dimethyl ether 95%, isobutane 5% and propane propellant gas) and disposable swab applicators. After attaching the swab to the bottle, the spray is pressed for approximately 15 seconds. Immediately, the swab is removed and applied to the cornea. Slow and soft movements are used, rolling over the entire pigmented surface until it reaches room temperature, after approximately 60 seconds. The cycle is repeated once more to complete the surgical procedure.

After cryosurgery, non-steroidal anti-inflammatory carprofen in the dosage of 4.4mg/kg (Rimadyl®, Pfizer Animal Health, Lincoln, USA) was administered orally, once a day (SID), for five days. Antibiotic eye drops of moxifloxacin 0.5% (Vigamox, Alcon, Brazil) and artificial tears of hydroxypropyl guar 8A and (Systane, Alcon, Brazil) were applied, four times a day (QID), for seven days. After seven days, if fluorescein stain was negative, topical moxifloxacin 0.5% and Dexamethasone 0.1% (Vigadexa, Alcon, Brazil) eye drops were started

Recebido: mai./2022.
Publicado: set./2022.

and applied, QID, for 21 days. All dogs continued topical therapy with tacrolimus 0.03% eyedrops and artificial tears, twice a day (BID), indefinitely after surgery. A follow-up occurred after 30 days, in four animals and six months, in three animals were made. All patients had initial depigmentation in the first week and after two weeks. However, after four weeks there was repigmentation (30–60%). Four dogs received follow-ups for four weeks and three dogs for six months (Fig. 02). All patients had partial repigmentation.

Figure 02: Eye image of a canine. (**Fonte:** Autoria própria, 2021)

Obs.: A = Image of right eye (RE) before cryosurgery; B = Image of RE. 7 days after cryosurgery; C = Image of RE. 28 days after cryosurgery; D = Image of RE. 6 months after cryosurgery.

RESULTS AND DISCUSSION

Corneal lesions in the brachycephalic breeds like a pug were quite commonly present and included corneal ulcers, degeneration, pigmentation and fibrosis. Pigmentary keratitis in Pug dogs was more resistant than in other brachycephalic breeds and when it affects the upper and lower medial quadrants, it impairs the vision of this breed. (LABELLE *et al.*, 2013; ANOOP *et al*., 2015; KUMAR *et al*., 2018; COSTA *et al*., 2021).

Pigmentary keratitis is more likely to be detected in older Pugs. In this case report, the mean age was 7.8 years (range 5–9 years). The median age of the dogs with pigmentary keratitis described in other studies was 4.1 years (MAINI *et al*., 2019) and in Pugs with ocular abnormalities an early mean age was found with a range of 2-8 years (KRECNY *et al*., 2015). In regards to gender, neutered female Pugs were 3.69 times as likely to not have pigmentary keratitis as were sexually intact female. No significant differences were detected for other comparisons of gender regarding the owner reports for detection of pigmentary keratitis (LABELLE *et al*., 2013).

In the present case report, all animals were neutered. Like the Pug, many other brachycephalic dog breeds have also been noted to develop pigmentary keratitis readily and without identifiable stimuli (VALLONE *et al*., 2017). The prevalence of pigmentary keratitis in United Kingdom Pugs in this study population was very high. Pigmentary keratitis was more likely to be detected in older Pugs and in those with limbal pigmentation and medial entropion

Recebido: mai./2022.
Publicado: set./2022.

of the lower eyelid, particularly if the medial entropion of the lower eyelid was severe (MAINI *et al*., 2019). The clinical aspects noted above were also observed in this study and, in the author's experience, corneal pigment was exacerbated in patients with severe keratoconjunctivitis sicca. In one study, corneal pigmentation was identified in 82% of Pugs examined. This study concluded that the corneal pigmentation in these Pugs was better described as pigmentary keratopathy, rather than pigmentary keratitis or corneal melanosis (LABELLE *et al*., 2013). For these reasons, the pug breed was chosen in the present case report. The cryosurgery technique has been used for over 40 years with liquid nitrogen and more recently with dimethyl ether. The last one is milder and its application in dogs of the breed has not yet been studied (STANLEY, 1986; AZOULAY, 2014).

Treatment of Pugs with pigmentary keratitis is poorly described in the peer-reviewed literature and mostly treated with topical administration of immunomodulator drugs such as cyclosporine A or tacrolimus (LABELLE *et al*., 2013). Some surgical treatments have already been proposed for the management of pigmentary keratitis as the soft X-ray irradiation combined with keratectomy. This is an effective treatment option for severe and advanced keratitis, superficial chronic and melanosis with significant visual impairment due to corneal pathology (ALLGOEWER and HOECHT, 2010). The surgical techniques commonly described in the literature have high costs or severe side effects. A less invasive technique for corneal pigment removal is cryosurgery (AZOULAY, 2014). As melanocytes sensitivity to cold is known, it could be a good alternative to reduce corneal pigmentation (RICKARDS, 1980; STANLEY, 1986).

Prando *et al*. used automated central lamellar superficial keratectomy for the treatment of chronic pigmentary superficial keratitis in dogs. Twenty one dogs (87.5%) recovered visual function. Three animals (12,5%) had granuloma and formation of central leucoma compromising cornea transparency and visual axis. In this case report with cryosurgery technique, no patient presented leucoma or other complications that caused vision loss. All cases presented good results.

Regarding the corneal vascularization and granuloma formation, the cryosurgery technique apparently has a good advantage. Corneal stroma and epithelium tissue is resistant to cold temperature, but underlying vessels and melanocytes which compound pigmentary tissue are sensitive and can necrotize under freezing leading to a better transparency (MERIDETH and GELLAT, 1980). Corneal blood vessels, especially those of recent development, can be destroyed by cryotherapy (RICKARDS, 1980). Soft cryosurgery causes no severe histologically detectable damage to cornea and conjunctiva in isolated pig eyes (BARACHETTI *et al*., 2020).

Other surgical treatments have been described in the literature, as diamond burr superficial keratectomy and medial canthoplasty in association with topical immunosuppressive agents. The authors demonstrated good results for this technique, but with few cases and a short follow-up (GRADILONE *et al*., 2012). Keratectomy for the management of pigmentary keratitis was also performed in Pug dogs (COSTA *et al*., 2021), which involved removal of the layer of diseased cornea and the area treated as a sterile corneal ulcer. These techniques revealed post-operative complications including conjunctival hyperaemia, neovascularisation, edema, fibrosis and repigmentation of the cornea. However, recurrence of pigmentation is the major complication seen that limits the successful outcome of keratectomy (QURESHI *et al*., 2020).

Recebido: mai./2022.
Publicado: set./2022.

Unlike superficial keratectomy, there is no obvious thinning of the cornea and the cryosurgical procedure undertaken in the present case report can be performed again if needed once because it does not require corneal layer removal. Comparatively, postoperative effects of cryosurgery included corneal edema resulting from epithelial injury caused by the dimethyl ether and conjunctival inflammation. In this study, these clinical signs disappeared over the 30 days of follow-up according to previous research (AZOULAY, 2014).

Stanley (1988) and Holmberg (1986) used liquid nitrogen successfully in the treatment of pigmentary keratitis in German Shepherd Dogs, however dimethyl ether is a milder form, an easier to perform technique than nitrogen, and is inexpensive. A cryogen of dimethyl ether 95%, isobutane 3% and propane 2% applied to the pigmented areas of each cornea under general anaesthesia has already been used in previous studies (AZOULAY, 2014). In this study, an aerosol cryogen with the same cryogenic agents above, and foam tip applicators are used, because a spray directly applied on the cornea would achieve deeper penetration and be less careful.

The prevalence of pigmentary keratitis in Pugs in previous studies was high. If pigmentary keratitis encroaches upon the visual axis, it can cause significant visual impairment and blindness (MAINI *et al*., 2019). This condition may have a genetic component and further studies are warranted to determine the aetiology (LABELLE *et al*., 2013). Pigmentary keratitis occurs due to centripetal migration of melanocytes from the limbal and perilimbal region and subsequent deposition of melanocytic pigment within the corneal epithelium and anterior stroma (VALONE *et al*., 2016). The current thinking is that the condition may have a genetic basis, and further studies are warranted to determine the aetiology (APPELBOAM, 2016). Nevertheless, it is known that dogs, especially Pugs, can go blind due to this disease (ALLGOEWER and HOECHT, 2010). For these reasons, the authors believe that cryosurgery can be listed as a form of treatment for pigmentary keratitis. Cryosurgery is effective like other procedures described in the previous studies. Cryosurgery was effective (HOLBERG, 1986; STANLEY, 1988) in the first 30 days like other techniques (PRANDO *et al*., 2022) (ALLGOEWER and HOECHT, 2010), however repigmentation also occurs in keratectomy (QURESHI *et al*., 2020).

Another advantage, observed in the study, was that this technique has short duration anaesthesia. Thereby, ocular centralization is essential to perform the technique properly. In the present study, a fixation suture was made in the bulbar conjunctiva and neuromuscular blockers were not used, although they could be recommended for centralization in ophthalmic surgery (AHN *et al*., 2013).

The cornea epithelium and sclera are resistant to cryosurgery. For this reason, the technique is quite safe, if it respects two freeze-thaw cycles in clinical studies (AZOULAY, 2014) and ex-vivo research (BARACHETTI *et al*., 2020). Cryosurgery has been researched in the human corneas affected by acanthamoeba and rabbits with corneal fungal infection in an experimental study. Its application has shown that it does not cause injury to keratocytes (CHEN *et al.*, 2015; HAGER *et al.*, 2016). Cryosurgery was applied to the cornea of three people who had herpes virus keratitis. After application, there was improvement in all cases without complications (FRAUNFELDER *et al.,* 2017*).* Conjunctival neoplasms were also treated with cryotherapy without causing damage to the cornea or sclera (OELLERS *et al.,* 2014). Ophthalmic cryotherapy selectively destroys certain tissues within the eye while sparing

Recebido: mai./2022.
Publicado: set./2022.

other vital areas (MEREDITH and GELLAT, 1980). According to Azoulay (2014), the destructive effect is cumulative, but the frequency of complications increases as the number of cycles increases. Most studies limit treatment to two cycles, because more than three cycles are not advantageous. For the safety of the patients studied, two cycles of freezing and thawing with dimethyl ether were performed. To minimize complications, frequent post-surgical ophthalmic evaluation is recommended, if discomfort and a positive fluorescein stain were observed in the first week in all dogs.

In the present study, no eyelid surgeries were performed to correct medial canthal entropion. These prominent eyes along with macroblepharon, or excessive long palpebral fissures do not allow for an adequate ocular coverage and lubrication (COSTA *et al*., 2021). Medial canthoplasty surgery may be indicated in any brachycephalic patients suffering from pigmentary keratitis or ulcerative keratitis (YI *et al*., 2006). The management of pigmentary keratitis with combined topical therapy and medial canthoplasty has proven more effective than topical therapy alone (ALLGOEWER *et al*., 2016). One of the hypotheses is that our patients have repigmented because of lacrimal insufficiency or keratoconjunctivitis sicca, medial entropion and breed predisposition. Pigmentation recurrence also results from the inability to control the concomitant presence of an underlying disease rather than the ineffectiveness of cryotherapy (AZOULAY, 2014). Further studies are required to evaluate the results of this technique associated with surgical correction of concomitant ophthalmopathies.

CONCLUSIONS

The technique used was easy to perform, has a low cryogen cost and has few undesirable or serious side effects. However, partial recurrence of corneal pigmentation occurred in all cases.

REFERENCES

AHN, J.; JEONG, M.; PARK, Y.; LEE, Y.; LEE, E.; KIM, S.; LEE, I.; SEO, K. Comparison of systemic atracurium, retrobulbar lidocaine, and sub-Tenon's lidocaine injections in akinesia and mydriasis in dogs. Veterinary ophthalmology, v.16, n.6, p.440-445, 2013.

ALLGOEWER, I.; HOECHT, S. Radiotherapy for canine chronic superficial keratitis using soft X-rays (15 kV). Veterinary Ophthalmology, v.13, n.1, p.20-25, 2010.

ALLGOEWER, I.; SAHR, S.; NEUMANN, K. Preliminary results of the evaluation of the long-term effect of different therapies for pigmentary keratitis of the pug. Veterinary Ophthalmology, v.19, n.6, p.21-43, 2016.

ANOOP, S.; DEVANAND, C.B.; SYAM, K.V.; MARTIN, K.D.; AJITHKUMAR, S.; GLEEJA, L.; GHOSH, K.N. Indian Journal of Veterinary Research, v.24, n.1, p.31-33, 2015.

APPELBOAM, H. Pug appeal: brachycephalic ocular health. Companion Animal, v.21, n.1, p.29-36, 2016.

AZOULAY, T. Adjunctive cryotherapy for pigmentary keratitis in dogs: a study of 16 corneas.

Recebido: mai./2022.
Publicado: set./2022.

Veterinary Ophthalmology, v.17, n.4, p.241-249, 2014.

BARACHETTI, L.; GIUDICE, C.; CESCON, M.; MORTELLARO, C.M.; FERRARI, R.; RAMPAZZO, A. The effects of soft cryotherapy on conjunctiva and cornea in isolated pig eyes and comparison with standard liquid nitrogen: A pilot ex vivo study. Veterinary Ophthalmology, v.23, n.3, p.544-551, 2020.

CHEN, Y.; YANG, W.; GAO, M.; BELIN, M.W.; YU, H.; YU, J. Experimental study on cryotherapy for fungal corneal ulcer. BMC Ophthalmology, v.15, n.1, p.1-9, 2015.

COSTA, J.; STEINMETZ, A.; DELGADO, E. Clinical signs of brachycephalic ocular syndrome in 93 dogs. Irish Veterinary Journal, v.74, n.1, p.1-8, 2021.

FEATHERSTONE, H.J.; RENWICK, P.; HEINRICH, C.L.; MANNING, S. Efficacy of lamellar resection, cryotherapy, and adjunctive grafting for the treatment of canine limbal melanoma. Veterinary Ophthalmology, v.12, n.1, p.65-72, 2009.

FRAUNFELDER, F.W.; ALLOJU, S.; PATEL, M. Liquid Nitrogen Cryotherapy Treatment of Herpes Simplex Epithelial Keratitis. Missouri Medicine, v.114, n.2, p.129-132, 2017.

GRADILONE, L.; ARTILES, S.; MENDOZA, E.; MORALES-FARINA, I. Clinical evaluation of the effect of diamond burr debridement in pigmentary keratitis in the dog: two case reports. Veterinary Ophthalmology, v.15, n.6, p.1-2, 2012.

HAGER, T.; HASENFUS, A.; STACHON, T.; SEITZ, B.; SZENTMÁRY, N. Crosslinking and corneal cryotherapy in acanthamoeba keratitis - a histological study. Graefe's Archive for Clinical and Experimental Ophthalmology, v.254, n.1, p.149-153, 2016.

HOLMBERG, D.L.; SCHEIFER, H.B.; PARENT, J. The cryosurgical treatment of pigmentary keratitis in dogs an experimental and clinical study. Veterinary Surgery, v.15, n.1, p.1-4, 1986.

KRECNY, M.; TICHY, A.; RUSHTON, J.; NELL, B.A. A retrospective survey of ocular abnormalities in pugs: 130 cases. Journal of Small Animal Practice, v.56, n.2, p.96-102, 2015.

KUMAR, T., PUNIA, M., AGNIHOTRI, D., SINDHU, N., JAIN, V.K. Incidence of Ophthalmic Affections in Dogs–A Short Study. International Journal of Current Microbiology Applied Science, v.7, n.9, p.1560-1565, 2018.

LABELLE, A.L.; DRESSER, C.B.; HAMOR, R.E.; ALLENDER, M.C.; DISNEY, J.L. Characteristics of, prevalence of, and risk factors for corneal pigmentation (pigmentary keratopathy) in Pugs. Journal of the American Veterinary Medical Association, v.243, n.5, p.667-674, 2013.

MAINI, S.; EVERSON, R.; DAWSON, C.; CHANG, Y.M.; HARTLEY, C.; SANCHEZ, R.F. Pigmentary keratitis in pugs in the United Kingdom: prevalence and associated features. BMC Veterinary Research, v.15, n.1, p.1-11, 2019.

MERIDETH, R.E.; GELATT, K.N. Cryotherapy in veterinary ophthalmology. The Veterinary Clinics of North America. Small Animal Practice, v.10, n.4, p.837–846, 1980.

OELLERS, P.; KARP, C. L.; SHAH, R. R.; WINNICK, M.; MATTHEWS, J.; DUBOVY, S. Conjunctival keratoacanthoma. British Journal of Ophthalmology, v.98, n.2, p.275-276, 2014.

Recebido: mai./2022.
Publicado: set./2022.

QURESHI, B.; MAHAJAN, S.K.; DEVI, N.U.; MOHINDROO, J.; PATHAK, D. Evaluation of superficial keratectomy for the management of pigmentary keratitis in Pug dogs. International Journal of Current Microbiology and Applied Sciences, v.9, n.10, p.3592-3598, 2020.

RICKARDS, D.A. Cryosurgery in small animal ophthalmology. The Veterinary Clinics of North America. Small Animal Practice, v.10, n.2, p.471-480, 1980.

STANLEY, R.G. Superficial stromal keratitis in the dog. Australian Veterinary Journal, v.65, n.10, p.321-323, 1988.

TEHRANI, S.; FRAUNFELDER, F.W. Cryotherapy in ophthalmology. Open Journal of Ophthalmology, v.3, n.4, p.103-117, 2013.

VALLONE, L.V.; ENDERS, A.M.; MOHAMMED, H.O.; LEDBETTER, E.C. In vivo confocal microscopy of brachycephalic dogs with and without superficial corneal pigment. Veterinary Ophthalmology, v.20, n.4, p.294-303, 2017.

WEB FRAUNFELDER, F. Liquid nitrogen cryotherapy for surface eye disease (An AOS thesis). Transactions of the American Ophthalmological Society, v.106, n.1, p.301-324, 2008.

YI, N.Y.; PARK, S.A.; JEONG, M.B.; KIM, M.S.; LIM, J.H.; NAM, T.C.; SEO, K. Medial canthoplasty for epiphora in dogs: a retrospective study of 23 cases. Journal of the American Animal Hospital Association, v.42, n.6, p.435-439, 2006.

Recebido: mai./2022.
Publicado: set./2022.